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SYNTHESIS OF CHALCONES AND 3, 5-DIARYL-Δ^2-ISOXAZOLINES

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ABSTRACT

A series of five different substituted chalcones (I_{a-e}) synthesized by Claisen-Schmidt condensation of 2-hydroxy-3-bromo-4-nitro-5-methyl acetophenone with different substituted aromatic aldehydes. By using these chalcones, five different 3, 5-diaryl-Δ^2- isoxazolines (II_{a-e}) were synthesized with hydroxylamine hydrochloride in pyridine containing few drops of piperidine. The synthesized compounds were characterized by IR and ^{1}H NMR spectral analysis.

Key words: Substituted chalcones, 3, 5-diaryl-Δ^2- isoxazolines.

INTRODUCTION

Heterocyclic compounds have so far been synthesized mainly due to the wide range of biological activities. Much attention has paid to the synthesis of heterocyclic compounds bearing nitrogen and oxygen containing ring system, like isoxazoline, pyrazoline and quinoline etc. mainly due to their higher pharmacological activity.

Chalcones are the important constituent of natural sources. They are first named by Kostanecki and Tambor[1]. Chalcones posses 1, 3-diaryl-1-ones skeleton, which withdraws the credit of biological importance. Chalcones are used as a well known intermediate for the synthesis of many heterocycles such as pyrimidines[2], pyrazolines[3], benzodiazepines[4], flavonones[5], isoxazolines[6], benzoxazolone[7], quinolines[8], indolinones[9] etc. thus being precursor for the wide range of such type of bioactive molecules. Chalcones itself exhibits biological activities such as antimalarial[10], cardiovascular[11], antimicrobial, anti-inflammatory[12] and also posses insecticidal[13] activity.

Syntheses of isoxazoline are great interest due to their exceptional biological activities. It have been reported that 3, 5-diaryl isoxazolines posses as a possible Anti-

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candida[14] agents. It has been reported that 3, 5-diaryl isoxazole derivatives posses as antimicrobial[15] activity. The isoxazolines derivatives also posses a anti-HIV[16], anticonvulsant[17] activity.

With this view we reported here the synthesis of novel Chalcones and 3, 5-diaryl-Δ^2-isoxazolines. These compounds were characterized by IR and ^{1}H NMR spectral analysis.

EXPERIMENTAL

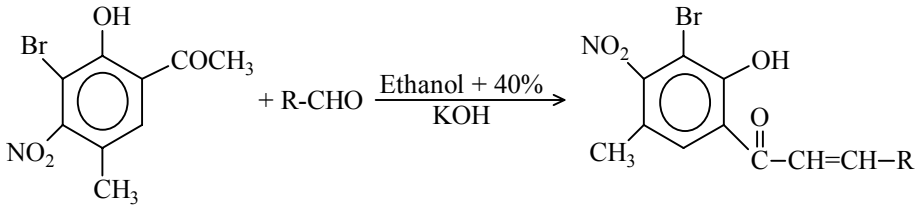
The purity of synthesized compounds were ascertained by thin layer chromatography on silica gel G using iodine vapours as detecting agents. All the Melting points reported were determined in open capillaries M.P. apparatus expressed in ^{0}C and are uncorrected. Chemicals and solvents were of highest purity commercially available. ^{1}H NMR spectra were recorded in the indicated solvent on Bruker AVANCE II 400 NMR spectrometer with TMS as internal standard. I.R. were recorded on Perkin-Elmer-841 spectrometer in KBr disc.

Synthesis of 2-hydroxy-3-bromo-4-nitro-5-methyl acetophenone (I)

p-cresyl acetate was prepared by known method. Then by fries migration 2-hydroxy-5-methyl acetophenone was obtained. This on bromination gives 2-hydroxy-3-bromo-5-methyl acetophenone. Which further on nitration gives starting compound i.e. 2-hydroxy-3-bromo-4-nitro-5-methyl acetophenone (I).

General method for synthesis of bromo-nitro substituted Chalcones (I_{a-e})

These compounds (I_{a-e}) were synthesized by Claisen-Schmidt condensation of 2-hydroxy-3-bromo-4-nitro-5-methyl acetophenone (I) 0.01 M by reacting it with five different substituted aromatic aldehydes (0.01 M) by reported method in ethanol using 40% KOH. The physical data of compounds (I_{a-e}) are given in Table 1.



(I) **(Ia-e)**

Scheme 1

The groups R are given in Table 1.

Table 1: Physical data of compounds (I_{a-e})

Compound No.	R'	Mol. Formula	M.P. (^oC)	Yield (%)
I_a	-p-OCH_3-Phenyl	$C_{17}H_{14}BrNO_5$	102	68
I_b	-m-NO_2-Phenyl	$C_{16}H_{11}BrN_2O_6$	205	70
I_c	p-$N(CH_3)_2$-Phenyl	$C_{18}H_{17}BrN_2O_4$	95	72
I_d	-2-Furyl	$C_{14}H_{10}BrNO_5$	105	67
I_e	-CH-$(CH_3)_2$	$C_{13}H_{14}BrNO_4$	91	61

Characterization of Compound (I_b)

IR (KBr) cm^{-1}: 3401 (broad hydrogen bonded Ar –OH), 2921 (Ar-H, C-H stretching), 2853 (Aliphatic C-H stretching of CH_3), 1644 (-C = O stretching), 1567 (-C = C), 1529 and 1356 (-NO_2 stretching), 595 (-C-Br), 1236 (C-O stretching).

^{1}H NMR ($CDCl_3$) Data: δ 3.0 (s, 3H, Ar-CH_3), 7.5 (d, 1H, =CH_A), 7.6 (d, 1H, =CH_B), 7.8-8.6 (m, 5H, Ar-H), 12.7 (s, 1H, Ar-OH).

Characterization of Compound (I_c)

IR (KBr) cm^{-1}: 3366 (Ar –OH), 2914 (C-H of Ar-H stretching), 1631 (-C = O stretching), 1602 (-C = C-), 1524 and 1371 (-NO_2 stretching), 1244 (-C-O), 546 (-C-Br).

^{1}H NMR ($CDCl_3$) Data: δ 2.28-2.3 (s, 3H, Ar-CH_3), 2.6 & 3.1 (S, 6H, -$N(CH_3)_2$), 6.6 (d, 1H, CH_A), 7.3 (d, 1H, CH_B), 7.4-7.8 (m, 5H, Ar-H), 12.8 (s, 1H, Ar-OH).

Characterization of Compound (I_d)

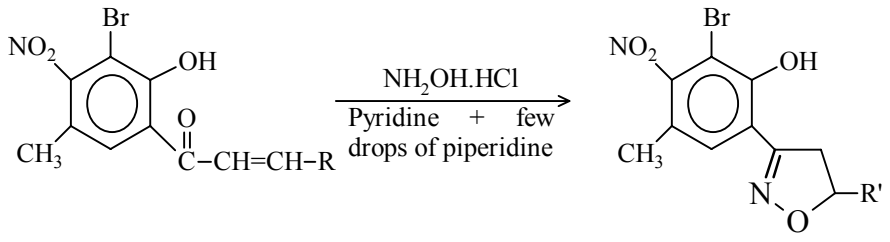
IR (KBr) cm^{-1}: 3399 (Ar –OH), 2917 (Ar-H, C-H stretching), 2851 (Aliphatic C-H stretching of CH_3), 1641 (-C = O), 1611 (-C = C), 1571 and 1361 (-NO_2 stretching), 1235 (-C-O-), 592 (-C-Br).

^{1}H NMR ($CDCl_3$) Data: δ 2.3 (s, 3H, Ar-CH_3), 6.5 (d, 1H, CH_A), 6.8 (d, 1H, CH_B), 7.4-7.7 (m, 4H, Ar-H), 13.4 (s, 1H, Ar-OH).

Synthesis of 3.5-diaryl isoxazolines (II_{a-e})

A mixture of bromo, nitro-substituted chalcone I_{a-e} (0.01 M) and $NH_2OH.HCl$ (0.02 M) were refluxed in 20 mL pyridine containing few drops of piperidine for 3-4 hours.

Cooled and acidified with 1 : 1 ice cold HCl, Thus compounds (II_{a-e}) were synthesized and recrystallised. Physical data are shown in Table 2.



(Ia-e) **(IIa-e)**

Scheme II

Table 2: Chemical data of the Compounds (II_{a-e})

Compound No.	R'	Mol. Formula	M.P. (°C)	Yield (%)
II_a	-p-OCH_3-PHENYL	$C_{17}H_{15}BrN_2O_5$	130	71
II_b	-m-NO_2-PHENYL	$C_{16}H_{12}BrN_3O_6$	155	66
II_c	p-$N(CH_3)_2$-PHENYL	$C_{18}H_{18}BrN_3O_4$	170	70
II_d	-2-Furyl	$C_{14}H_{11}BrN_2O_5$	125	64
II_e	-CH-$(CH_3)_2$	$C_{13}H_{15}BrN_2O_5$	162	60

Characterization of Compound (II_b)

IR (KBr) cm^{-1}: 3395 (Ar-OH stretching), 2922 (Ar-C-H), 2853 (-C-H of CH_3), 1529 and 1349 (-NO_2), 1616 (-C = C), 1693 (-C = N), 1262 (-C-O), 1188 (C = N-O), 577 (C-Br).

^{1}H NMR ($CDCl_3$) Data: δ 2.3 (s, 3H, Ar-CH_3), 3.4 (dd, 1H, CH_A), 3.6 (dd, 1H, CH_B), 4.5 (dd, 1H, CH_X), 7.2-8.4 (m, 5H, Ar-H), 12.3 (s, 1H, Ar-OH).

Characterization of Compound (II_c)

IR (KBr) cm^{-1}: 3392 (Ar-OH stretching), 2917 (Ar-C-H), 1524 & 1364 (-NO_2), 1604 (-$CH_2$of iso ring), 1258 (-C = N-O), 1455 (C = C), 1264 (-C-O of phenol), 568 (C-Br), 854 and 812 (p-Substituted ring).

^{1}H NMR ($CDCl_3$) Data: δ 2.2 (s, 3H, Ar-CH_3), 2.9 (s, 6H, -$N(CH_3)_2$), 3.1(dd, 1H, CH_A), 3.8 (dd, 1H, CH_B), 5.1 (dd, 1H, CH_X), 6.5-8 (m, 5H, Ar-H), 8.5 (s, 1H, Ar-OH).

RESULTS AND DISCUSSION

Thus the bromo-nitro-substituted Chalcones (I_{a-e}) and 3, 5-diaryl-Δ^2- isoxazolines were synthesized through the route as shown in reaction schemes. Physical data of compounds are shown in Table 1 and 2. The structure of synthesized compound I_b, I_c , I_d and II_b, II_c were confirmed on the basis of I.R. and NMR spectral analysis.

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